Early Brain Development and Human Development

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The early years of human development establish the basic architecture and function of the brain.[1] This early period of development, (conception to ages 6-8), affects the next stage of human development, as well as the later stages. We now better understand, through developmental neurobiology, how experience in early life affects these different stages of development.[1] Poor early development affects health (physical and mental), behaviour and learning in later life.

The architecture and function of the brain is sculpted by a lifetime of experiences which affect the architecture and function of neurobiological pathways.[1,2] Stimuli transmitted to the brain through sensing pathways pre- and post-natally, as well as in later stages of life, differentiate the function of neurons and neural pathways.

The billions of neurons in an individual's brain have the same gene coding (DNA). The neurons differentiate for their diverse functions (e.g. vision, hearing, touch, behaviour, etc) through epigenetics.[1,3,4,2] Epigenetics is the molecular and cellular process that governs the function of genes. These processes include *DNA methylation*, changes in *chromatin structure*, non-coding *RNA*s and *RNA editing*.[3,4,5] Those working in epigenetics have concluded that understanding the mechanisms that regulate gene differentiation and function will be a critical component of neurobiological research in the 21st century.[3,4,2] The epigenetic changes in neuron function affect neurobiological pathways that influence health (physical and mental), behaviour and learning.[2,6,4] The effects of epigenetics on gene function begins at conception and continues during in utero development, and development following birth.

Experiences that affect brain development through the sensing pathways include sound, touch, vision, smell, food, thoughts, drugs, injury, disease and other factors.[2,4]

Identical twins have the same DNA in their neurons (*genotype*) but will not have the same experience, leading to differences through epigenetics in gene expression (*phenotype*). Identical twins can have a 20 to 30% difference in behaviour as adults (phenotype).[7] This difference is probably related to epigenetic affects on neuron function in early development. As a result of these studies, there is increasing interest in how epigenetics could be a factor in schizophrenia, bi-polar disorders and conditions such as Attention Deficit Hyperactivity Disorder (ADHD) as well as physical health in adult life.[2,8,6,9] Studies have shown that there is *hypermethylation* of the *DNA promoter region* in the *hippocampus* of suicide victims with a history of abuse and neglect in early life[10] but not in suicide victims with no early abuse or neglect.

Animal studies have demonstrated epigenetic affects on gene function. The normal mouse *agouti gene* leads to brown pigmented fur and normal body size. The variant agouti gene is dominant over the normal agouti gene and results in obese mice with yellow fur.[11] It was found that when pregnant mothers with the variant agouti *allele* were fed methyl-donor dietary supplements to methylate in utero, the variant agouti gene regulator, the offspring showed extensive methylation of the gene and were of normal colour and not obese. The coat colour and size of these newborn mice correlated with the amount of methylation of the variant agouti gene.

In rats, behaviour responses to stressful situations are correlated with the number of *glucocorticoid* receptors in the brain's hippocampus.[4] The more glucocorticoid receptors in the hippocampus, the better the adult rat is able to regulate the glucocorticoid hormones and stress. The rats exposed to strong licking and grooming by their mothers after birth, lose the methylation of the glucocorticoid receptor gene, leading to good receptor formation in the hippocampus. The animals with good receptor formation show a better regulated stress pathway and are easy to handle, while the animals with decreased glucocorticoid receptor capacity are easily stressed. In these studies, the researchers found that the administration of a compound (*trichostatin A*) removed the epigenetic effect and normalized the stress behaviour of the rats.[4]

Retrospective studies in humans have shown that development in the utero period and infancy influences risks for adult diseases (*type II diabetes*, hypertension, heart attacks, obesity, cancer and aging).[2,6,12] The Kaiser Permanente studies in California[13] found that adults with mental health problems, addiction, obesity, type II diabetes, coronary artery disease, and other conditions in adult life had poor early child development.

If these and other problems related to development are contributed to by epigenetic effects in early life, can early intervention prevent or easily reverse the processes?

The work of Grantham-McGregor and colleagues has demonstrated that stunted children at birth, if given nutrition and stimulation after birth, can approach the performance of control children after 24 months.[14] These studies are compatible with the hypothesis that epigenetic effects initiated during early development can be prevented or reversed by good nutrition and stimulation. The orphanage studies in Romania show that children placed in middle class homes in Great Britain, Canada and the US who were in the orphanages for eight months or longer had, at 11 years of age, in contrast to the children adopted within four months after birth, abnormal brain development (small brain), abnormal electroencephalograms (EEGs) and low metabolic activity.[15] The children adopted late showed abnormal behaviour (ADHD, aggression, and quasi autism) and poor cognitive development (low IQ) at age 11. Some children in the orphanages were randomized to foster parenting in Romania and compared to children left in the orphanages.[16] When this study was done, the majority of the children had spent at least two years in the orphanages. The mean IQ of the orphanage children was 71; the IQ of children placed in foster care was 81; and for children brought up by their biological parents, the IQ was 110.[16] Children placed in foster care early were approaching normal human development but this was not occurring for children placed in foster care after the age of two.

In the Abecedarian study in North Carolina, African American children at four months of age were randomized into two groups: an intensive yearly preschool program or no specific program.[17] When the children entered the school system, the children in each group were randomized to either a special three-year education program or the standard school program. The special three-year program produced some improvement in the reading and numeracy function of the children not in the preschool program but the effect was small and gradually lost. The children given the preschool program and the standard school program showed much better school performance but there was some loss of performance by age 21. The children given the preschool program plus the three-year education program showed the biggest gains and this was sustained.

We now know that the quality of child development at the time of school entry predicts performance in school programs.[18,19]

Results from developmental neurobiology studies and animal and human studies provide strong evidence that early neurobiological development affects health (physical and mental), behaviour and learning in the later stages of life. Countries that provide quality universal early development programs for families with young children tend to out-perform countries in which the early development programs are chaotic.[1]

Cuba established in the mid-1970s a poly-clinic structure for prenatal and post-natal care (nutrition, healthy development and stimulation). The outstanding improvement in the health status of Cubans in contrast to other Caribbean and Latin American countries may well be related to the quality of the poly-clinic program on early development (according to a conversation with A. Tinajero in 2009). It is possible that this program, which began with pregnancy, is also an important reason why the Cubans substantially out-perform the other Latin American countries in the UNESCO studies of language and literacy and numeracy in grades 3 and 6.

We now know that nurture in early life as well as nature is important in early human development and that nurture in the early years has major effects on learning in school and physical and mental health throughout the life cycle.

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